

REMARKS

Claims 1-22 are of record pending in this case and stand rejected. Claims 1-9 and 11-16 are hereby amended, and claims 17-22 are hereby cancelled. No other claims are currently added or canceled. Accordingly, claims 1-16 remain pending in the application. Reexamination and reconsideration of claims 1-16 are respectfully requested.

Note, no new matter is believed to be added by any of the amendments hereof or herein. Moreover, any matter cancelled or otherwise no longer in the present claims due to amendment, cancellation or otherwise is intended to be so cancelled or otherwise outside the present scope without prejudice to potential pursuit through continuation or otherwise.

Applicants note that the Preliminary Amendment, submitted on August 23, 2006, was effectively not entered. Thus, the publication version of the application, published on May 8, 2008, fails to incorporate the majority of the changes set forth in the Preliminary Amendment of August 23, 2006 and generally resembles the original PCT application. Applicants' current amendments to the claims reconcile this matter by entering the substantive changes of the Preliminary Amendment while retaining the claim numbering of the publication version of the application. However, the Office Action of November 20, 2008 appears to use the claim numbering of the Preliminary Amendment rather than the claim numbering of the publication version of the application. Applicants understand the dichotomy, and will address the objections to the claims in this Response by noting the Office Action/Preliminary Amendment claim number objected to, followed by the correct publication version number of the claim at issue in parentheticals.

Priority

Applicants note the comments on priority as set forth in the paragraph for cross-references to related applications. Applicants hereby amend that paragraph to remove the language found objectionable. Applicants thus submit that this objection has been obviated and/or traversed and can thus be withdrawn. Action to this end is respectfully requested.

Information Disclosure Statement

Applicants acknowledge that the Office Action notes that the IDS received on January 25, 2007 and March 19, 2007 are in proper form and are being considered.

Drawings

Applicants acknowledge that the Office Action notes that the drawings filed on August 23, 2006 are acceptable.

Specification - Informalities

Applicants note the comments on the specification and the purported informalities related to the PCT application numbers not previously provided; particularly as on page 6 of the original application. The specification has been amended hereby to correct the informalities. Applicants further note that evidence was requested in the Office Action indicating that the “PCT numbers being amended … [are] the same PCT[s] which the applicants had contemplating in incorporation by reference.” See footnote 1, page 3 of the Office Action. Applicants note that such evidence is provided in that the title of this application is the same in the original text of the current specification as well as in/on the corresponding PCT application presenting the serial numbers hereby amended into this specification. Moreover, Applicants respectfully note that each of these other two PCT applications referred to here share the same inventorship (Jensen, Thomsen and Veltman), ownership (Thomsen Bioscience A/S), filing date (25 February 2005) and priority date (26 February 2004). It is therefore evident that these are companion cases filed simultaneously by the same people and having intended reference one to another. Applicants thus respectfully submit that these objections have been obviated and/or traversed and can thus be withdrawn. Action to this end is respectfully requested.

Claim Rejections 35 U.S.C. § 112

Applicants note the rejections of claim 10 (claim 7) and claims 15-19 (claims 18-22) for a variety of specific alleged informalities. Applicants note that all of these informalities have been addressed by amendments or cancellation herein, and thus, respectfully note that all of these rejections have been obviated and/or traversed and can thus be withdrawn. Actions to these ends are respectfully requested.

Rejections Under 35 U.S.C. § 102(b)

Claims 15-17 (claims 18-20 in the publication version, and in this amendment) stand rejected under 36 USC 102(b) as purportedly being anticipated by Mainelis et al. (Reference

number 54 from the IDS of January 25, 2007; hereinafter “Mainelis 1999”). Claims 15-19 (claims 18-22, here) stand rejected under 36 USC 102(b) as purportedly being anticipated by Mainelis et al. (Reference number 56 from the IDS of January 25, 2007; hereinafter “Mainelis 2002”).

Applicants note that all of the foregoing claims, claims 15-19 in the Office Action (claims 18-22, here in this amendment), have been cancelled, and therefore respectfully present that the foregoing rejections are moot.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-3 (claims 1, 14 and 15, here) and claims 5-14 (claims 2-11, here) stand rejected under 35 USC §103(a), as purportedly being unpatentably obvious over various uses of Birmingham et al. (U.S. Patent No. 5,989,824; hereinafter “Birmingham”) in view of Mainelis et al. (Reference number 56 from the IDS of January 25, 2007; hereinafter “Mainelis”). Claims 4 (claim 16, here) and claims 15-19 (claims 18-22, here) stand rejected under 35 USC §103(a), as purportedly being unpatentably obvious over Birmingham in view of Mainelis and further in view of Johns, et al. (Reference number 47 from the IDS of January 25, 2007; hereinafter “Johns”). Applicants respectfully note the obviation of and/or respectfully traverse these rejections for at least the reasons discussed below.

As a preliminary matter, Applicants respectfully note, in short, that Applicants agree that Birmingham does not have “first and second [] electrode[s]” nor is a chamber positioned so that at least part of the sample chamber is between the first and second electrode, and that a potential is applied to the first and second electrode so as to assist electrostatic collection of the biological sample into the chamber; nor does Birmingham explicitly disclose that the distance between the first and second electrode is at most 20 mm, claim 2; nor does Birmingham provide for “providing a liquid sample in the sample chamber, which liquid sample comprises a bacterial spore”; nor does Birmingham disclose that sample chamber has a volume of at most 500 μ L. Applicants’ claim 1, elements a, b and c.

Birmingham rather uses “ionized discharges” and “gases”; not electrodes, nor electric fields and not liquids. Thus, Birmingham does not therefore teach or suggest the purported

corresponding elements of Applicants' claims and consequently does not provide a proper basis for rejection under section 103, whether on its own or in view of Mainelis, alone or together with Johns.

On this, a first essential in patent law is that the proper interpretation of an applicant's claim terms is that they are to be construed in view of their specifications, see Philips v. AWH discussion herein; Phillips v. AWH Corp., 415 F.3d 1303, 1314, 75 USPQ2d 1321, 1327 (Fed. Cir. 2005). Here, Applicants' independent claim 1 specifically involves, as defined in Applicants' specification, a liquid sample, electrodes and an electric field generated by and between the electrodes which have specific meanings which are definitively different than those of the gas and ionized discharges asserted from Birmingham (any possibility for an electric field to be associated with an ionized discharge, notwithstanding; i.e., Birmingham does not disclose electric field existence, nor use, and doesn't enable either existence or use; and moreover, nonesuch was asserted in the Office Action, by implication or otherwise).

More particularly, the Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." In re Am. Acad. of Sci. Tech. Ctr., 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must "conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 CFR 1.75(d)(1). MPEP 2111 is in accord, the claims are to be interpreted by their broadest reasonable interpretation in view of the specification.

Similarly, a reference disclosure is necessarily limited by what is actually taught or suggested thereby; i.e., limited to what is enabled thereby. The disclosure in an asserted reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003). See also, In re Hoeksema, 399 F.2d 269, 158

USPQ 596 (CCPA 1968) where it is noted for chemistry-type cases that mere naming of a compound in a reference, without more, cannot constitute a description of the compound.

Note, this concept of “undue experimentation” is substantially the same as that used for judging the enablement of an applicant’s disclosure; and, on this, MPEP 2164.03 Relationship of Predictability of the Art and the Enablement Requirement is instructive. In particular, there it is noted that:

in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work.

What this means here is that Applicants’ use of the words “liquid”; “electrodes” and “electric field” in Applicants’ specification and claims are directed to very discrete and different elements than the gaseous media and ionizing discharge generator as set forth in or suggested by Birmingham. The asserted elements of Birmingham have different meanings from Applicants’ claim words and have different functional and characteristic results therefrom as well.

More particularly, these elements provide for different chemistries and physical activities; particularly, in a primary example, to different rupturing processes; i.e., the rupturing process of Birmingham is quite different from the rupturing process of the present application. Birmingham uses gases and an ionizing discharge generator to generate ionized discharges and uses these ionized discharges to rupture the biological particles in a gaseous medium; e.g., “air [] caused to flow adjacent to a member energized with an ionizing potential[;] … [t]he ionized air [] then [being] directed at the cell.” Birmingham, col. 2, lines 61-65. Quite distinctly, a bacterial spore in Applicants’ case is exposed to the electric field (see step c) of claim 1) established between the first and second electrodes (see step c) of claim 1), where it has surprisingly been found that the particle is ruptured more gently, and with lower energy consumption, than if the ionized discharge process of Birmingham were used. In this regard Applicants have shown that the

morphological changes observed in the coat of biological particles may be indicative of a process that more resembles electroporation rather than complete lysis. Ionized fluids (i.e. gases) created by discharges are very disruptive, which may be an advantage if killing the bacterial spores is the only objective. However, it is a disadvantage if a subsequent, sensitive, biochemical analysis or culture of the organism or spore should be performed, such as in Applicants' case. Moreover, the lower energy consumption of Applicants' development is favorable relative to Birmingham, when Applicants' development is implemented in portable detection devices.

Still furthermore, in the third paragraph of page 8 of the Office Action it was alleged that Birmingham discloses contacting the collected biological particle with a **liquid agent**. However, this is not correct, and not enabling thereof. Rather, Birmingham does not disclose any liquids during the rupturing process. Instead, Birmingham only discloses gases such as air and argon. Gases do not teach, suggest or enable a "liquid." Certainly, Birmingham uses the word "fluid"; however, it only describes gases such as air and argon, and does not therefore enable movement toward liquid use (as described further below). Birmingham neither discloses a liquid sample containing the bacterial spores, nor rupturing the bacteria spores in the liquid sample.

Additionally on this issue of liquids and the failure of enablement thereof, Birmingham could not lead the person skilled in the art to the presently claimed subject matter since ionized discharges do not form in liquid; i.e., Birmingham's use of the word "fluid" could only enable use in gases, liquids not being feasible with the ionized discharges thereof, at least not without undue experimentation. Thus, this is not a mere naming of broader subject matter (mere naming fluids when only gases were intended), nor a mere description of subject matter which is insufficient (mere lacking of description of liquids), nor even is it merely an issue of undue experimentation or relative unpredictability of the art (would liquids predictably work?) nor a mere chemistry issue (inherent unpredictability); rather, this is a situation where the asserted substitution would apparently not, on its face, work. Again from MPEP 2164.03 there is failure of enablement of the reference "especially ... where the statement is, on its face, contrary to generally accepted scientific principles." Since ionized discharges do not form in liquid, Birmingham could not have enabled use in/with liquids. Disclosure of the species of air in the genus of fluids did not enable any liquid species.

It is therefore clear that the presently-claimed subject matter is non-obvious in view of the prior art of Birmingham. Mainelis and Johns do not cure these failures of Birmingham (and indeed are not asserted for such purposes), and thus, the present claims are allowable over any of the purported combinations of these references.

Claims 1-3 (claims 1, 14 and 15, here) and claims 5-14 (claims 2-11, here)

More particularly, claims 1-3 (claims 1, 14 and 15) and claims 5-14 (claims 2-11) stand rejected under 35 USC §103(a), as allegedly being obvious over Birmingham in view of Mainelis. Applicants respectfully disagree.

In Applicants' present development, the miniaturized, electrostatic particle collection in a sample chamber having a relatively small volume provides substantial differences over the cited references. First of all, Applicants' device/method offers a better degree of concentration of the biological particles, both due to the close proximity of the first and the second electrode and due to the small volume of the sample chamber. Furthermore, due to the small volume of Applicants' sample chamber and the high degree of concentration, it becomes feasible to suspend the collected particles in a liquid and to perform analysis directly on this liquid without any of the time-consuming enrichment steps, which are set forth in Mainelis. Besides the time-saving advantage, the liquid handling of the present system also becomes simpler, easier to control, and easier to integrate with other microsystem technologies. Finally, the small size of the chamber allows significantly lower power consumption than possible in a design similar in size to the designs referenced by the Office Action.

There are a number of incompatibilities between Birmingham and Mainelis, which would prevent one skilled in the art from pursuing such a combination.

First of all, as set forth in detail above, Birmingham generally relates to an apparatus for lysing of bacterial cells or spores, which apparatus uses ionized **fluids, only exemplified by ionized gases**. Birmingham does not disclose contacting the collected biological particles with a **liquid**, which is erroneously suggested on page 7, lines 1-4 of the Office Action. There is a genus-species relationship between fluid (genus) and liquid (species) and the mere mention of

fluid when gas was used does not enable a liquid. Thus, neither Birmingham nor Mainelis disclose contacting the collected biological particles with a liquid, and the combination of these documents therefore cannot lead one skilled in the art to the present development.

Mainelis generally describes an electrostatic precipitator for a bioaerosol sampler for collection of airborne microorganisms on a collection medium. However, Mainelis fails to provide any teaching on how to extract biological material from the sampled microorganisms, but appears to use the sampler for culturing only. Thus, neither Birmingham nor Mainelis, nor a combination of the two, disclose exposing a bacterial spore in a liquid sample to an alternating electric field.

Additionally, Mainelis teaches an agar layer necessarily between the two electrodes, but Birmingham prefers that the particles are present on a metal coupon. Birmingham appears to require ionizing charges over the biological particles, and the Applicants deem it very difficult, if not impossible, to create useful ionizing charges in a controlled manner over the agar-covered electrode of Mainelis.

Finally, neither Mainelis nor Birmingham disclose a sample chamber having a volume of at most 500 μ L, and it is questionable whether any of the technologies disclosed in Birmingham or in Mainelis would work with sample chamber of such small volume. For example, it is unclear how the agar should or would be deposited in such a small volume. It would appear that there is a significant risk that the agar would clog up a small-volume sample chamber as defined in Applicants' devices, systems and methods.

It is therefore fair to conclude that the skilled artisan would not reach the development of the present claims 1-3 (claims 1, 14 and 15, here) and claims 5-14 (claims 2-11, here) without substantial inventive activity, and the claims are therefore non-obvious.

Moreover, Mainelis does not cure the lacking of Birmingham in also not disclosing or suggesting a substitution to or change from the Birmingham system toward "a liquid sample" or "electrodes" with an "electric field" therebetween. There is no motivation to or from either Birmingham or Mainelis to substitute two electrodes and an associated electric field

therebetween for an ionizing discharge generator (Birmingham doesn't suggest that it may have or want a substitute for the ionizing discharge generator, and Mainelis doesn't suggest adaptation of its electrodes into a system like Birmingham's). Moreover, there is no suggestion, nor assertion to achieve a liquid reagent mixture by asserted combination of Mainelis with Birmingham. Mainelis is not even asserted for such a purpose. Birmingham fails to enable a liquid sample, and Mainelis is not asserted to cure this failure. Thus, there is no motivation or suggestion for combination of Birmingham with Mainelis to result in Applicants' claimed subject matter, as particularly set forth in independent claim 1 as well as all claims dependent therefrom, and thus, such alleged combination fails to render obvious Applicants' claims having such. Claims 1-3 (claims 1, 14 and 15) and claims 5-14 (claims 2-11) are thus patentable over Birmingham in view of Mainelis.

Applicants still furthermore respectfully submit that Applicants' developments would indeed NOT be obvious to one skilled in the art for the following reasons. “[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” In re Kahn, 441 F. 3d 977, 988 (Fed. Cir. 2006). The law of obviousness requires that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. KSR International Co. v. Teleflex Inc., 550 U.S. 398, 82 USPQ2d 1385 (2007) and see, e.g., MPEP 2143, *inter alia* (note, KSR explicitly retained the teaching, suggestion, motivation, TSM, test); see also In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (concentrating upon what the prior art actually ‘taught’, ‘expressed’, ‘conveyed’, and/or ‘spoke of’).

Merely combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art. KSR; and see, United States v. Adams, 383 U.S. 39, 42-43, 51-52, 148 USPQ 479, 480, 483-84 (1966) (stating that “[d]espite the fact that each of the elements . . . was well known in the prior art, to combine them as did Adams required that a person reasonably skilled in the prior art must ignore the teaching away of the prior art”). “When the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be nonobvious.” KSR v. Teleflex, *supra*, at 82 USPQ2d 1395.

In this case, Applicants' claimed developments of claim 1 include a liquid sample comprising a bacterial spore, subjected to an electric field established by and between two electrodes; however, Mainelis does not suggest substitution in or for any part of Birmingham to achieve this; nor vice versa; Birmingham does not suggest or motivate the elimination of the ionizing discharge generator and substituting something other. If Mainelis is cited merely for its teaching of an electric field and electrodes; there nevertheless remains no suggestion for the liquid sample.

In either case, the Office Action does not however, demonstrate an appropriate suggestion or motivation to the alleged substitution/combination. There is no mechanism detailed, nor steps provided, nor any other information regarding how such would be accomplished or why one would want to make this particular substitution. Note, generalized motivations regarding the advantage of producing "portable devices for military usages" *inter alia*, for achieving end functionalities or greater efficiencies do not provide the type of particularized motivations necessary for the teaching, suggestion, motivation (TSM) test affirmed in KSR; i.e., the motivation for substitution has to be specific, what element substituted where or why, not merely some generalized motivation toward a greater efficiency overall. Therefore, Mainelis does not provide the motivation for substitution to achieve the combination as defined and claimed by Applicants and that Birmingham lacks, and thus Mainelis does not cure the failures of Birmingham.

In short, this situation is not one of simple substitution, nor is it one of a simple 'upgrade'. See, cf., KSR, 82 USPQ2d at 1399 (discussing 'upgrading Asano with a sensor'). Applicants' presently claimed developments involve a combination, not subject to nor being a simple addition, replacement, mounting or an upgrade from Birmingham.

Indeed, there is no teaching or suggestion of an expectation of success from such an alleged modification of Birmingham with Mainelis. See KSR and MPEP 2143. Birmingham and Mainelis have completely operable systems or methods which expect no modification for their particular type of success. It would be unexpected for any of the foregoing to be made over or modified to generate non-suggested elements within the system or method. There is no suggestion or motivation that any particular element is either absent from or needing substitution

from either or both of Birmingham and Mainelis; nor that any particular element could or should be incorporated into or onto the Birmingham device, with no rational basis for suggestion how the electrodes of Mainelis would be used to make the substitution. There is no such expectation, thus, no suggestion or motivation for the asserted modification(s). No reasonable expectation of success comes from any of those references. See, e.g., MPEP 2143.01, 2143.02.

In the instant case, a person of ordinary skill in the art having common sense as described in KSR at the time of the invention would not have reasonably looked to Mainelis to solve a problem not even announced in or by either Birmingham or Mainelis. An artisan having common sense at the time of Applicants' developments would not even be concerned with the ionizing discharge generator of Birmingham, let alone how such might be replaced using a substitute set of electrodes whether like those in Mainelis or otherwise; let alone from where and in what manner such skilled persons might be directed to use of a liquid reagent. Thus, Applicants respectfully submit that the rejection of claims 1-3 (claims 1, 14 and 15) and claims 5-14 (claims 2-11) on Birmingham and Mainelis falls short.

The rejections of claims 1-3 (claims 1, 14 and 15, here) and claims 5-14 (claims 2-11, here) are thus obviated or traversed and can and should be withdrawn. Action to this end is respectfully requested.

Claims 4 (claim 16) and claims 15-19 (claims 18-22)

Similarly, claims 4 (claim 16, here) and claims 15-19 (claims 18-22, here) stand rejected under 35 USC §103(a), as purportedly being obvious over Birmingham in view of Mainelis and further in view of Johns. As a preliminary matter, Applicants also note that claims 15-19 (claims 18-22, here) have been cancelled by this Response to Office Action, and Applicants thus address their responses to claim 4 (claim 16).

Johns discloses a method of detecting *Bacillus anthracis* in spores by use of PCR but does not relate to miniaturized electrostatic collection of biological particles in a small-volume sample chamber, and can therefore not bring the skilled artisan any closer to the present invention than Birmingham or Mainelis.

And, as was the case for Mainelis, Johns does not cure the initial lackings of Birmingham; and, indeed, it was not even asserted for such purpose. Thus, for the same reasons Mainelis failed to supplement Birmingham; all such reasons being incorporated herein as if fully set forth here, Johns also fails to provide all of the missing elements presented in Applicants' claims and thus Applicants' claims are patentable hereover. There is still no teaching or suggestion of the two electrode electric field nor of a liquid sample. This rejection can thus be withdrawn.

Moreover, Applicant does hereby challenge and respectfully request art citations for the assertion of official notice for the alleged teaching of a chip, and/or other so-called miniature-integrated devices which conduct a plurality of biological assays, and apparatus which analyze such devices, with particularly any relevance hereof toward and/or teaching/suggestion or motivation therefrom toward the presently-claimed subject matter. Applicants cite Rule 104 (37 CFR 1.104) for this purpose, and note that absent a citation of authority, Applicants should receive instead a declaration or affidavit of the Examiner based on the Examiner's experience in the field for demonstration of the proposition.

The rejections of claims 4 (claim 16) and claims 15-19 (claims 18-22) are thus obviated and/or traversed and can and should be withdrawn. Action to this end is respectfully requested.

The rejections of claims 1-13 are thus obviated and/or traversed and can and should be withdrawn. Action to this end is respectfully requested.

Double Patenting – Obviousness Type

Applicants note the provisional double-patenting rejections of the current claims over the claims of the co-pending application. Applicants agree that these claims are not identical, but do not agree that they are obvious in view of each other, one way or the other. However, in the interests of speedy prosecution, and not in admission of any obviousness one way or the other, Applicants agree that upon the notation of allowable subject matter, they would file a duly signed

Terminal Disclaimer to obviate these rejections. These rejections would thus be subject to and may now properly be withdrawn.

CONCLUSION

Applicants note that all rejections are obviated or traversed and respectfully request that they thus be withdrawn. A timely Notice of Allowance is requested to be issued in this case. Applicants believe that no fees or petitions, other than the extension fee/petition set forth above, are due with this filing. However, should any such fees or petitions be required, please consider this a request therefore and authorization to charge Deposit Account No. 02-2093 as necessary.

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Respectfully submitted,

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